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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/656,084	09/06/2000	Barry N. Kreiswirth	19124.0002	8869

23517 7590 02/05/2007

BINGHAM MCCUTCHEN LLP
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EXAMINER	
ZEMAN, MARY K	
ART UNIT	PAPER NUMBER
1631	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/656,084	KREISWIRTH ET AL.	
	Examiner	Art Unit	
	Mary K. Zeman	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,7,8,10-14,16,17,21-36,38 and 42-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-5, 7, 8, 10-14, 16, 17, 21-36, 38 and 42-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments filed 9/28/06 have been entered and fully considered.

Claims 1, 3-5, 7, 8, 10-14, 16, 17, 21-36, 38 and 42-44 are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32, 33, 34-36 38 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's argue that they choose not to be bound to any definition of the term remote in the context of the rejected claims. These arguments to do provide clear boundaries of what is claimed. The examiner offered multiple definitions for the term which cannot all exist in one system at the same time. MPEP 2173: "when there is more than one definition for a term, it is incumbent upon applicant to make clear which definition is being relied upon to claim the invention. Until the meaning of a term or phrase used in a claim is clear, a rejection under 35 U.S.C. 112, second paragraph is appropriate." "remote" is a variable term and it is unclear how far apart the parts must be to satisfy the claim limitations.

Applicant's arguments do not address how the remote facility is to obtain the samples. How does a facility take samples from a patient? It would appear that individuals or health care workers *within* a facility would take the samples, and not the remote facility itself, and not the claimed system. A system is an interlinked set of physical elements such as a computer, display and output; or article of manufacture and controller.

Similarly, the metes and bounds of the term "remote" in claims 34 -36 are unclear. At what point is the facility remote from where the sequencing is performed? On a different table? In a different room? In a different building?

Applicant's arguments with regards to claim 33 are incorrect. The claim is not drawn to a system, but to software code stored on a computer readable media. The metes and bounds of the software code of claim 33 are unclear. How does a software code obtain samples from a patient? Software code cannot physically obtain a sample. Further, software code cannot sequence a sample.

It is unclear how the limitation of claim 44 further limits the system of claim 32. Applicant's arguments are not persuasive, as a method limitation does not further limit a system structure. Where in the system does the sequencing occur? What is required to perform the sequencing? A hardware element? A software element? A scientist?

The metes and bounds of claim 38 are entirely unclear. How can an infection be identified before it occurs? It may be able to be predicted, but it can't be identified until it exists. Applicant arguments are not persuasive. The term "outbreak" is not limited no mean more than one patient.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-5, 8, 10-14, 16, 17, 21-27, 32-36, 38, 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over CDC plan 1998, in view of Frothingham (1998).

Applicant's arguments have been fully considered, but are not persuasive. Applicant alleges the Examiner builds on impermissible hindsight, and alleges an improper state of the art at the time the invention was made. These arguments are not persuasive. Applicant argues there is no express motivation to combine the cited references, however, such an express motivation is not required in a determination of obviousness. Motivation to combine prior art references may exist in the nature of the problem to be solved (Ruiz at 1276, 69 USPQ2d at 1690) or the knowledge of one of ordinary skill in the art (National Steel Car v. Canadian Pacific Railway Ltd., 357 F.3d 1319, 1338, 69 USPQ2d 1641, 1656 (Fed. Cir. 2004)). See MPEP § 2143.01. Applicant argues many limitations which are not present in the pending claims, and provides no evidence that one of skill in the art would not have considered the combination of references cited. Applicant's arguments cannot take the place of evidence. MPEP 2129 and 2144.03.

The rejection clearly sets forth the state of the art at the time the invention was made. The rejection states the conclusions and suggestions of the CDC plan 1998 in combination with the conclusions and suggestions of Frothingham (1998). The CDC plan clearly sets forth that newly discovered methods of identification of specific bacteria are to be incorporated and added to the existing system for tracking and controlling outbreaks of infection. Frothingham clearly identifies their method as being superior for identifying the specific type of bacteria, through methods meeting the limitations of the rejected claims.

CDC Plan "Preventing Emerging Infectious Diseases; a strategy for the 21st Century, October, 1998" discloses methods of tracking and controlling infectious diseases. The document discloses Surveillance, and Response, Prevention and Control. Diseases of varying types including infectious diseases, foodborne diseases, airborne and zoonotic diseases, and diseases of travelers are all discussed. The Centers for Disease Control is an agency comprised of many elements, such as the National Center for Infectious Disease which can process patient samples and provide data. The CDC is linked to state and local health departments (which can obtain samples) comprising medical professionals, and to research facilities which comprise scientific personnel. Page 14 of the disclosure is a summary of the CDC plan. Surveillance is defined as "the ongoing systematic collection, analysis interpretation and dissemination of health data... Epidemiologists use these data to detect outbreaks; characterize disease transmission patterns by time, place and person; evaluate prevention and control programs and project future

health care needs." (page 17). The collection of samples meets step (1) of the method. The analysis and interpretation encompasses steps (2-4) of the method. Detecting the outbreak and characterization meet the limitations of steps (5 and 6) and the dissemination meets the "warning" step of the claimed method. The FoodNet is an illustration of a system with a centralized database which performs the disclosed method. The FoodNet collects data obtained from patient specimens, compares and tracks the data. The FoodNet can provide warnings as to infection spread or outbreak. EMERGEncyIDNET , IDSA EIN, WHO Polio Lab Network, and GeoSentinel are other networked systems for tracking and controlling infections. The patient specimens can be obtained from Emergency departments, Infectious Disease Practicioners, and Clinics. Objects (food) and Object locations (place of manufacture, or sale, or consumption) as well as patient locations can all be tested and/or tracked. Issues of patient confidentiality are discussed. Samples are compared against local and international data. Warnings are specifically noted in the GeoSentinel summary as "travel advisories".

The CDC Plan specifically indicates that molecular fingerprinting techniques are to be used to distinguish between strains or isolates of bacteria, fungi viruses or parasites. M. tuberculosis is a specifically contemplated infection. Methods used include comparing sequences and comparing the sizes of fragments. These tests are to be performed on patient samples, as well as objects and/or locations such as water supplies, food shipments, infected animals, etc. This plan creates a "real-time, on-line" capacity to identify and compare certain strains of bacteria. Particular subsystems specified by this plan include geographic information systems and computer programs that detect subtle variations of surveillance data that may indicate disease outbreaks. Early Warning systems are also disclosed to disseminate information on a wide scale.

At page 27, the plan specifically encourages the development of new diagnostic testing methods. The creation of tools for the collection and analysis of risk factor data, geographic information systems and remote sensing technologies and specifically disclosed.

The CDC Plan does not disclose the sequencing of the VNTR (Variable Number of Tandem Repeats) regions of the bacteria in the samples.

Frothingham et al. (1998, PTO-1449) discloses methods of assessing genetic diversity of a pathogen through the sequencing of the VNTR region of the pathogen. Frothingham et al.

obtain patient samples and sequence the VNTR region of the pathogen M. Tuberculosis. Primers are used to amplify the VNTR, then its size and sequence are determined. Comparison of the presence, size and sequence of these regions between samples provided a measure of diversity. Numbers of direct repeat sequences, the level of insertion or the level of deletion can be determined. Multiple distinct strains were identified and discriminated. The methods were determined to be stable and reproducible. Frothingham specifically notes that this procedure can be used in strain differentiation for diagnosis of infection and evolutionary studies. Other considered uses are epidemiological investigation, identification of outbreak-related strains and recognition of cross contamination. This method is an improvement over prior diagnostic techniques such as molecular fingerprinting. The previous art recognized standard, the molecular fingerprinting test, for M Tuberculosis had poor discriminatory power.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have incorporated the VNTR sequencing of Frothingham in the CDC Plan for controlling and tracking infection. One of skill in the art would have been motivated to incorporate the methods of Frothingham, as they were shown to be an improvement over known techniques. The improved discrimination between types of a pathogen allow for more specific identification of the etiology of an outbreak, and better tracking of specific related infections. The high level of one of skill in the art of microbiology and medicine indicate that the methods could have reasonably been performed. One of skill in the art would have had a reasonable expectation of success at combining the methods of Frothingham with the CDC Plan, as the CDC Plan specifically provides for the incorporation of new specific diagnostic testing. Therefore the entire invention, as a whole, would have been prima facie obvious, absent evidence to the contrary.

Claims 1, 3-5, 7, 8, 10-14, 16, 17, 21-36, 38 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over CDC plan 1998, in view of Van Belkum (1998).

Claim 7 specifies that the method tests for VNTR in the Protein A or coagulase genes of S Aureus. Claims 28-31 add multiple region sequencing.

Applicant's arguments have been fully considered, but are not persuasive. Applicant alleges the Examiner builds on impermissible hindsight, and alleges an improper state of the art

at the time the invention was made. These arguments are not persuasive. Applicant argues there is no express motivation to combine the cited references, however, such an express motivation is not required in a determination of obviousness. Motivation to combine prior art references may exist in the nature of the problem to be solved (Ruiz at 1276, 69 USPQ2d at 1690) or the knowledge of one of ordinary skill in the art (National Steel Car v. Canadian Pacific Railway Ltd., 357 F.3d 1319, 1338, 69 USPQ2d 1641, 1656 (Fed. Cir. 2004)). See MPEP § 2143.01. Applicant argues many limitations which are not present in the pending claims, and provides no evidence that one of skill in the art would not have considered the combination of references cited. Applicant's arguments cannot take the place of evidence. MPEP 2129 and 2144.03. The rejection clearly sets forth the state of the art at the time the invention was made. The rejection states the conclusions and suggestions of the CDC plan 1998 in combination with the conclusions and suggestions of Van Belkum (1998). The CDC plan clearly sets forth that newly discovered methods of identification of specific bacteria are to be incorporated and added to the existing system for tracking and controlling outbreaks of infection. Van Belkum clearly identifies their method as being superior for identifying the specific type of bacteria, through methods meeting the limitations of the rejected claims.

CDC Plan "Preventing Emerging Infectious Diseases; a strategy for the 21st Century, October, 1998" discloses methods of tracking and controlling infectious diseases. The document discloses Surveillance, and Response, Prevention and Control. Diseases of varying types including infectious diseases, foodborne diseases, airborne and zoonotic diseases, and diseases of travelers are all discussed. The Centers for Disease Control is an agency comprised of many elements, such as the National Center for Infectious Disease which can process patient samples and provide data. The CDC is linked to state and local health departments (which can obtain samples) comprising medical professionals, and to research facilities which comprise scientific personnel. Page 14 of the disclosure is a summary of the CDC plan. Surveillance is defined as "the ongoing systematic collection, analysis interpretation and dissemination of health data... Epidemiologists use these data to detect outbreaks; characterize disease transmission patterns by time, place and person; evaluate prevention and control programs and project future health care needs." (page 17). The collection of samples meets step (1) of the method. The analysis and interpretation encompasses steps (2-4) of the method. Detecting the outbreak and

characterization meet the limitations of steps (5 and 6) and the dissemination meets the "warning" step of the claimed method. The FoodNet is an illustration of a system with a centralized database which performs the disclosed method. The FoodNet collects data obtained from patient specimens, compares and tracks the data. The FoodNet can provide warnings as to infection spread or outbreak. EMERGEncyIDNET , IDSA EIN, WHO Polio Lab Network, and GeoSentinel are other networked systems for tracking and controlling infections. The patient specimens can be obtained from Emergency departments, Infectious Disease Practicioners, and Clinics. Objects (food) and Object locations (place of manufacture, or sale, or consumption) as well as patient locations can all be tested and/or tracked. Issues of patient confidentiality are discussed. Samples are compared against local and international data. Warnings are specifically noted in the GeoSentinel summary as "travel advisories".

The CDC Plan specifically indicates that molecular fingerprinting techniques are to be used to distinguish between strains or isolates of bacteria, fungi viruses or parasites. S Aureus, and M tuberculosis are specifically contemplated infections. Methods used include comparing sequences and comparing the sizes of fragments. These tests are to be performed on patient samples, as well as objects and/or locations such as water supplies, food shipments, infected animals, etc. This plan creates a "real-time, on-line" capacity to identify and compare certain strains of bacteria. Particular subsystems specified by this plan include geographic information systems and computer programs that detect subtle variations of surveillance data that may indicate disease outbreaks. Early Warning systems are also disclosed to disseminate information on a wide scale.

At page 27, the plan specifically encourages the development of new diagnostic testing methods. The creation of tools for the collection and analysis of risk factor data, geographic information systems and remote sensing technologies and specifically disclosed.

The CDC Plan does not disclose the sequencing of the VNTR (Variable Number of Tandem Repeats) regions of the bacteria in the samples, or to perform this particular analysis onf the protein A or coagulase genes of S Aureus.

Van Belkum (SSR Loci in Prokaryotic Genomes; MMBR 1998 62:275-293: PTO 1449) discloses methods of assessing genetic diversity of a pathogen through the sequencing of the VNTR region of the pathogen. Van Belkum obtain patient samples and sequence the VNTR

region of the protein A gene and/or coagulase gene of S Aureus. (see pages 283-284.). Primers can be used to amplify the VNTR, then its size and sequence are determined. Comparison of the presence, size and sequence of these regions between samples can provide a measure of diversity. Numbers of direct repeat sequences, the level of insertion or the level of deletion can be determined. Multiple distinct strains were identified and discriminated. The methods were determined to be stable and reproducible. Van Belkum specifically notes that this procedure can be used in strain differentiation for diagnosis of infection and evolutionary studies. The coagulase is a major phenotypic species determinant in S Aureus. Van Belkum notes that repeat elements enable bacteria to respond to diverse environmental factors, which appear to be related to pathogenesis, and these elements are extremely important in the study of adaptive behavior. Van Belkum note the successful use of PCR mediated SSR amplification, followed by size study and using sequencing for the pathogens of H influenzae and C albcans. These repeats lend themselves to the development of novel assays suited for strain identification and definition of strain relatedness.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have incorporated the repeat sequence region sequencing of Van Belkum in the CDC Plan for controlling and tracking infection. One of skill in the art would have been motivated to incorporate the methods of Van Belkum, as they were shown to be an improvement over known techniques. The improved discrimination between types of a pathogen allow for more specific identification of the etiology of an outbreak, and better tracking of specific related infections. The high level of one of skill in the art of microbiology and medicine indicate that the methods could have reasonably been performed. One of skill in the art would have had a reasonable expectation of success at combining the methods of Van Belkum with the CDC Plan, as the CDC Plan specifically provides for the incorporation of new specific diagnostic testing. Therefore the entire invention, as a whole, would have been prima facie obvious, absent evidence to the contrary.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary K Zeman whose telephone number is (571) 272 0723

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272 0811. The fax phone number for the organization where this application or proceeding is assigned is 571 273 8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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1/31/07